World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

MEDICAL DEVICE FOR DEVELOPMENT OF BIODEGRADABLE POLYMERIC NANOCAPSULES

Syed Gouse Firoz*, A. Sow Reddy, K. Jyothi, Y. Mohana Pravallika, B. Naveen, S. Sri Latha and K. Sai Teja

Associate Professor, Dept. of Pharmaceutics, A.M Reddy Memorial College of Pharmacy Petlurivaripalem, Narasaraopeta, Guntur Dt. AP 522601.

***Corresponding Author: Syed Gouse Firoz**
Associate Professor, Dept. of Pharmaceutics, A.M Reddy Memorial College of Pharmacy Petlurivaripalem, Narasaraopeta, Guntur Dt. AP 522601.

Article Received on 09/11/2023 **Article Revised on 29/11/2023** **Article Accepted on 19/12/2023**

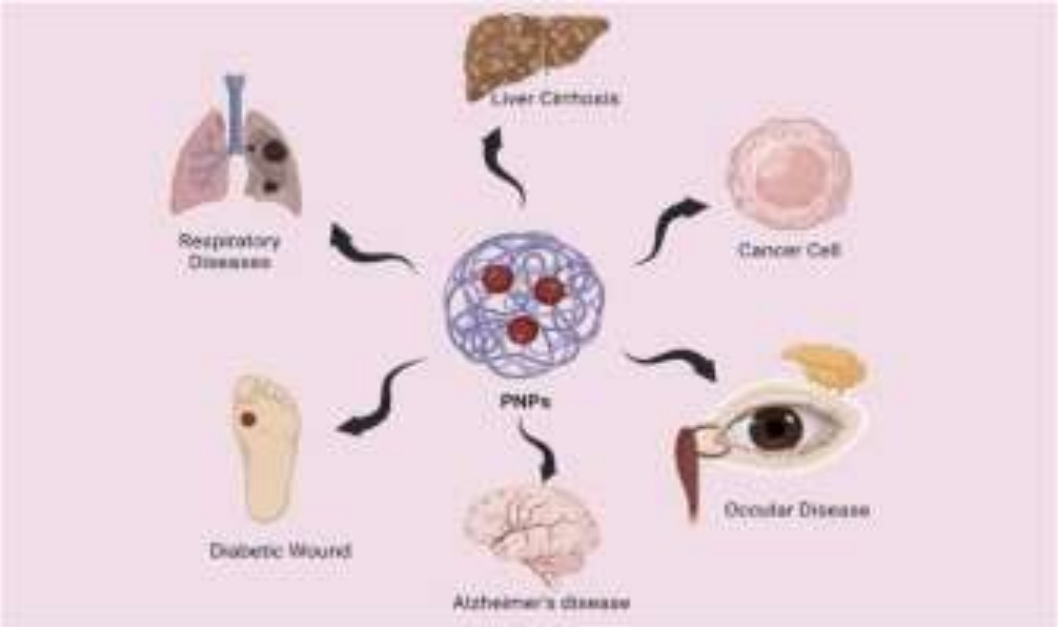
ABSTRACT

The development of modern medicine has been significantly impacted by the use of polymers as biomaterials. The potential use of biodegradable polymeric as carriers for a variety of therapeutic applications is being explained by numerous researchers worldwide. The limitations of traditional dosage forms are addressed by employing polymers with enhanced bioavailability, biocompatibility, and decreased toxicity in conjunction with tailored and altered drug delivery techniques. As a result, nanomedicines are regarded as a novel class of pharmaceutical. The most significant discoveries concerning surface characterization and surface modification techniques are discussed from 1990 to the middle of 2000.

KEYWORDS

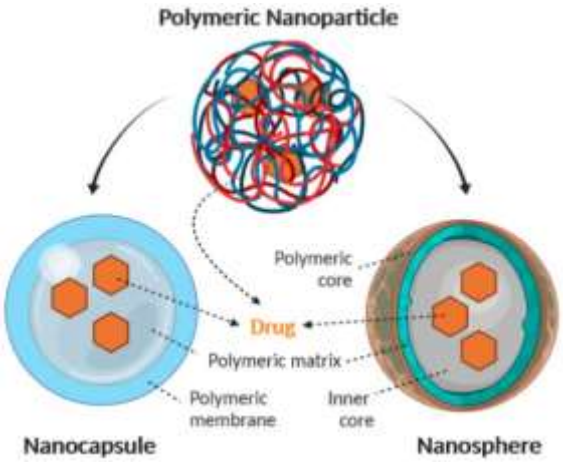
- Polymers
- Biomaterials
- Biodegradable
- Nano medicines
- Bioavailability
- Bio compatability
- Drug delivery

GRAPHICAL ABSTRACT



INTRODUCTION

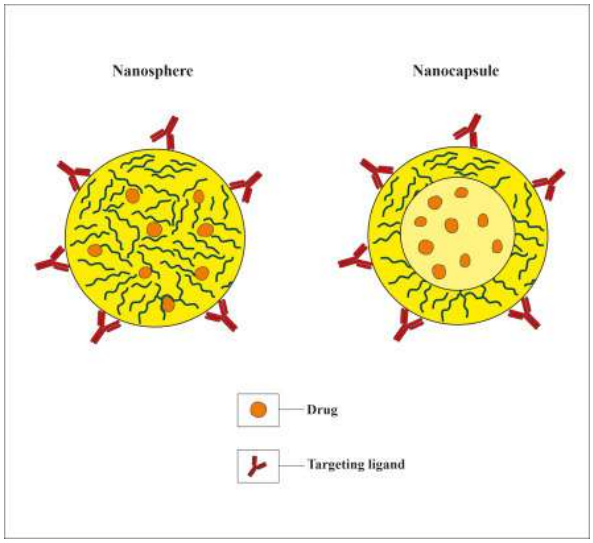
Magic bullets loaded with tiny drugs were a concept put forth by Paul Ehrlich a century ago. Subsequently, Kumar and Banker came up with the idea for a submicron drug delivery system in 1996. Liposomes and micro/nanoparticles are the most often studied of these carriers. Recent years have seen a rapid advancement in the application of nanotechnology in biomedical science, particularly in the fields of medicine, disease prevention, diagnosis, and treatment. The sizes of these nanoparticle-based platforms, which range from 1 to 100 nm, include PNPs, functionalized NPs, nanomedicine, and nanofibers. PNPs have been extensively studied as drug carriers. Since the 1980s, PNPs have been used in drug delivery, with various polymers being used to distribute and transport different kinds of medications. The most extensively



Schematic representation of the structure of nano capsules and nanospheres (arrow stands for the presence of drug/bioactive within the nanoparticles)

NANOCAPSULES HOW TO DELIVERING TARGETED CELLS?

The oil-filled core of nano capsules, surrounded by polymeric membranes, contains medications that, given the right circumstances, can release their contents through a reaction to biological, chemical, thermal, or environmental stimuli. Colloidal nano capsules are produced by depositing premade polymers (PLA, PLGA, PCL, and PEG) between surfaces. It works well for administering medications that are hydrophobic. Lipid nano capsules have been applied to rat tumor cases that are resistant to many drugs. Hureauxetal have proposed a novel hybrid protein-lipid polymer nano capsule of 180 nm as a nontoxic drug for codelivery of transcription factor p53 and lipophilic drug paclitaxel to induce HeLa cell apoptosis; this gives incentive to try using nano capsules for drug delivery to RCC, even though not much work has been done on this topic (78).

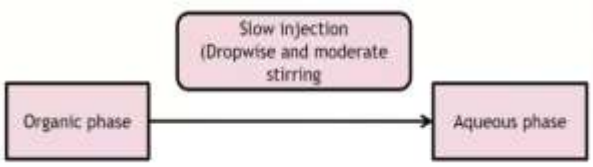


METHODS OF NANO CAPSULES PREPARATION

There exist six methods for the nano capsules preparation: nanoprecipitation, emulsion–diffusion, double emulsification, emulsion-coacervation, polymer coating and layer by-layer method.

❖ Nano precipitation

The process of precipitating a preformed polymer from an organic solution and diffusing the organic solvent into an aqueous medium is known as nanoprecipitation, or solvent displacement method (Fessi et al. 1989; Barichello et al. 1999; Galindo-Rodriguez et al. 2004; Ganachaud and Katz 2005). The dissolution of the polymer in an intermediately polar solvent causes the precipitation of nanospheres. This phase is added to an aqueous solution that has a surfactant stabilizer in it. A colloidal suspension may form quickly as a result of polymer deposition on the organic solvent-water interface brought on by the solvent's rapid diffusion (Quintanar-Guerrero et al. 1998). Phase separation is carried out using a different solvent, which is also not a solvent of the.



GENRAL FORMULA

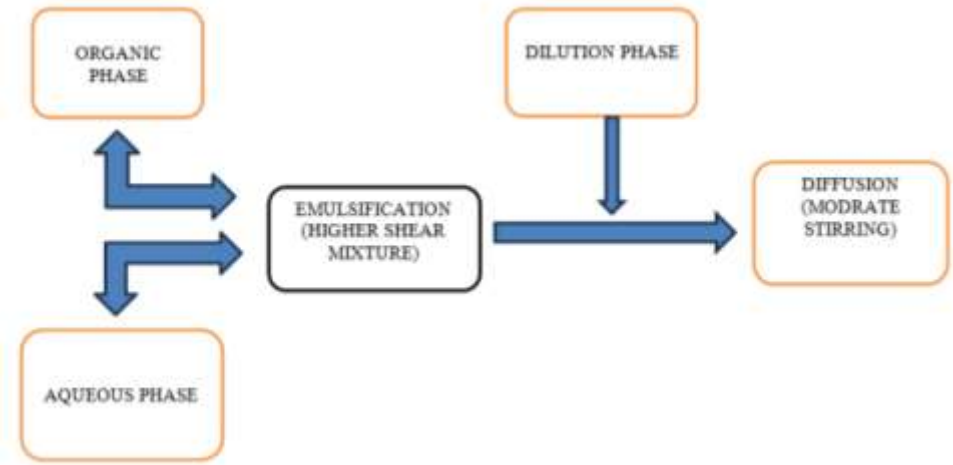
Materials	Suggested Composition
Active substance	10-25mg
	0.2-0.5% of solvent
Oil	1.0-5.0% of solvent
W/O Surfactant	0.2-0.5% of solvent
solvent	25ml
stabilizer	0.2-0.5% of solvent
Non solvent	50ml

EXAMPLES OF DRUGS

drugs	polymer	Oil core	solvent	activity
Indomethacin	PCL Mw 60 kda	Mineral oil	acetone	Anti inflammatory

❖ EMULSIFICATION SOLVENT DIFFUSION

Diffusion of Emulsification Solvent The partial miscibility of an organic solvent with water and the crosslinking between the reactive functional amine groups of chitosan and aldehyde groups are prerequisites for the emulsification solvent diffusion technology's production of chitosan nanoparticles. For the manufacture of chitosan particles, cross-linkers such as formaldehyde and glutaraldehyde were often utilized. Further Recently, vanillin has also been employed as a cross-linker for the synthesis of chitosan particles in order to circumvent the toxicity of formaldehyde and glutaraldehyde. Vanillin, which is extracted from vanilla pods, is a flavoring compound that is widely utilized in the food, beverage, and cosmetic sectors (Memişoğlu et al. 2003). Using a high shearing force, an organic phase is injected into a chitosan solution containing a stabilizing agent, and the mixture is then homogenized.



GENERAL FORMULA

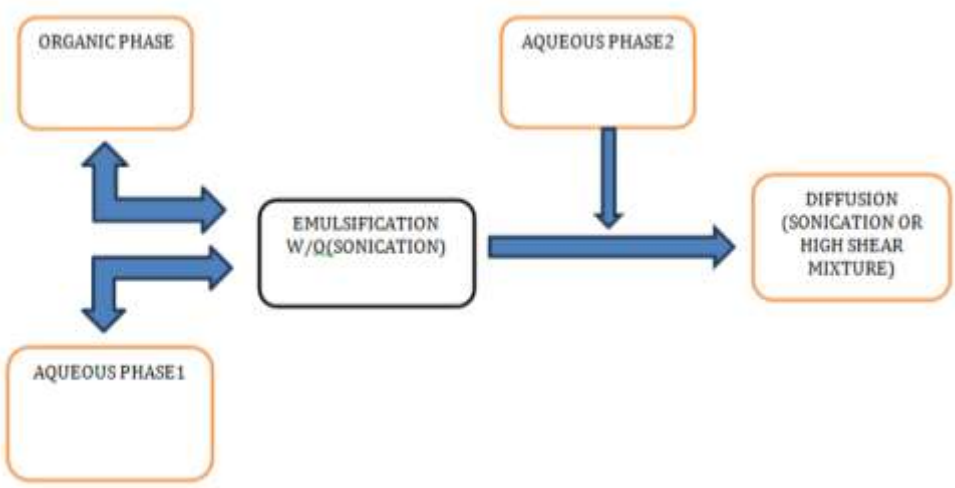
MATERIALS	SUGGESTED COMPOSITION
Active substance	10-50mg
oil	1-2% of solvent
polymer	2.5-5% of solvent
Inner phase solvent	10ml
stabilizer	2-5% of solvent
External phase solvent	200ml

EXAMPLES OF DRUG

DRUGS	Inner Phase			External Phase		Dilution Phase	Use
	Polymer	Core	Solvent1	Stabilizer Agent	Solvent 2		
Indomenthacine	PCL Mw 10	Caprylic triglycerid	Ethyl acetate	Pva Poloxamer	Water	Water	Anti inflammator

DOUBLE EMULSIFICATION METHOD

Water-oil-water emulsion and oil-water-oil emulsion are the two main types of double emulsions, which are complex heterodisperse systems known as "emulsions of emulsions" (Nagarwal et al. 2009) (Garti 1997). An additional phase layer divides the inner dispersed droplet from the outer liquid phase. The dispersed phase is an emulsion in and of itself. Using two surfactants—a hydrophobic one to stabilize the interface of the internal emulsion and a hydrophilic one to stabilize the external interface of the oil globules for water-oil-water emulsions—double emulsions are prepared in a two-step emulsification process. Ultrasound is also used to create the second emulsion, and the stabilizing agent is added to stabilize the nanocapsule dispersion. The solvents are eliminated in the final stage by vacuum extraction or evaporation, leaving.



GENERAL FORMULA

MATERIALS	SUGGESTED COMPOSTIONS
AInner aqueous	
a. Active substance	0.5-25mg
b. water	0.15-0.5
organic phase	
a. Polymer	5-10% of organic solvent
b. W/O surfactant	5-7% of organic solvent
c. solvents	1.5-5ml
3) External aqueous phase	
a. stabilizer agent	1-5% of external aqueous phase
b. water	2-5ml

EXAMPLES OF DRUGS

DRUG	W1 PHASE	ORGANIC PHASE	W2 PHASE	USE
Insulin	Active ingredient, water	PLA Mw 10 kDa, DCM, sorbitan monoleate	Polysorbate 80,60 or 20 glycerin: water	Antidiabetic

❖ **LAYER- BY- LAYER**

Creating thin polymeric layers on surfaces and thus capsules is made possible by the Layer-by-Layer self-assembly method, which offers several advantages. This technique can use a variety of materials and is simple and affordable. The fundamental idea behind the Layer-by-Layer (LbL) technique is to create thin, homogeneous multilayers on the original substrates by means of electrostatic interactions between oppositely charged polyelectrolytes or other materials. A single layer of thorium ions was adsorbed onto a monomolecular layer of barium stearate by Langmuir in 1941, demonstrating the concept of adsorption of ions onto a surface to form a single layer (Ariga et al. 2019). Iler used this technique in the 1960s to layer negatively charged silica colloids and positively charged alumina fibrils alternately onto.

❖ **Emulsion-coacervation method**

The main application of the emulsion-coacervation process is the preparation of nanocapsules from naturally occurring polymeric materials. Gelatin and sodium alginate have been utilized thus far, however artificial polymeric materials could also be employed. Through the use of ultrasound or simple stirring, an organic phase and an aqueous phase are emulsified on-the-whelming. Subsequently, a coacervation process is carried out using electrolytes containing a sodium alginate–calcium chloride system, water miscible non-solvent (Lertsutthiwong et al. 2008), a dehydration agent containing a gelatin–isopropanol–sodium sulfate system (Krause and Rohdewald 1985), or temperature modification utilizing triblock terpolymer in the synthesis of gold nanocapsules (Lutter et al. 2008). Lastly, further crosslinked steps are added to the coacervation.

❖ **Polymer-coating method**

The preparation of the nano emulsion template is the first step in Prego et al.'s proposed polymer coating method, which involves coating the water/oil nano emulsion surface with polymer deposition. Unlike the emulsion coacervation method, the polymers are added in the continuous phase, and their precipitation onto the nano emulsion droplets is triggered by solvent evaporation. They begin their process with an organic phase that contains the active ingredient, oil, lecithin as a surfactant,

and acetone as a solvent. Next, they move on to an aqueous phase that contains the stabilizing agent and an aqueous polymer-coating solution. The o/w nano emulsion is created by solvent displacement after the organic and aqueous phases are combined with moderate stirring. Under vacuum, the solvents are allowed to evaporate until they

EXAMPLES OF DRUGS

Drugs	Organic Phase	Aqueous Phase	Coating	Use
Salmon Calcitonin	Active Ingredient Caprylic Triglycerides, Acetone	Poloxamer 188, Water	Chitosan Oligomers	Calcium Regulator

APPLICATION

- Delivery of drugs; food enhancement; nutraceuticals; materials that promote self-healing
- A nanocapsule containing insulin produced encouraging pharmacological results.
- Betaxolol-loaded isobutyl cyanoacrylate nanocapsules were created through interfacial polymerization and glucoma treatment.
- The antiviral medication ganciclovir is used to treat cytomegalovirus infections.

ADVANTAGES OF NANOCAPSULES

Increased bioavailability of drug; Lower irritation at the site of action; Control and sustain release of drug at the site of localization; Higher dose loading; Site specification action; Better patient compliance; Greater protection from degradation during storage and administration.

DISADVANTAGES

The toxicity of using poly vinyl alcohol as a detergent on a large scale Restricting targeting capabilities and stopping therapy are not feasible.

A direct impact on heart and vascular function, alveolar inflammation, cytotoxicity, pulmonary inflammation, and pulmonary carcinogenicity are all examples of the disruption of autonomic balance caused by nanoparticles.

CONCLUSION

The development of methodological formulation through a variety of techniques, principally interfacial polymerization and interfacial nano-deposition, is aided by nanocapsules.

They can also be released as monodisperse particles with distinct optical, electrical, magnetic, and biochemical characteristics. Nanomaterials have been applied extensively in the fields of molecular diagnostics, electronics, pharmaceuticals, and biochemistry. Their high reproducibility and wide range of applications, owing to their micronized size, make them suitable for use in life science applications. Nanocapsules are an effective application in a variety of fields, including waste water treatment, cosmetics, agrochemicals, and genetic engineering. They can also be used to encapsulate biological cells, oil nanoparticles, adhesives, inorganic or organic catalysts, surface polymers, and enzymes.

Smart drugs can be created using nanocapsules.

REFERNCES

1. Adriana RP, Letıcia SF, Rodrigo PS, Alberto MD, Edilson VB, Tania MHC, et al. Nano capsule@xerogel microparticles containing sodium diclofenac: A new strategy to control the release of drugs. *Int J Pharm.*, 2008; 358(1-2): 292-95.
2. Adriana RP, Leticia C, Graziela M, Leonardo US, Nadya PD and Silvia SG. Structural model of polymeric nanospheres containing indomethacin ethyl ester and in vivo antiedematogenic activity. *Int J Nanotechnol*, 2007; 4(5): 454-67.
3. Benita. S. Microparticulate drug delivery systems: release kinetic models. Microspheres, Microcapsules and Liposomes (the MML Series). R. Arshady (Ed.), Citrus Books, London, 1998; 255-278.
4. Daniel TC, Polina BS and Kimberly AD. Investigating Lyophilization of Lipid Nanocapsules with Fluorescence Correlation Spectroscopy. *Langmuir*, 2010; 26(12): 10218-22.
5. Deutsch E, Libson K, Vanderheyden JL, Ketring AR and Maxon HR. The chemistry of rhenium and technetium as related to the use of isotopes of these elements in therapeutic and diagnostic nuclear medicine. *Int J Rad Appl Instrum B.*, 1986; 13(4): 465-77.
6. K. Arnold, T.S. Balaban, M.N. Blom, O.T. Ehrler, S. Gilb, O. Hamoe, *et al.* Electron autodetachment from isolated nickel and copper phthalocyanine-tetrasulfonate tetraanions: isomer specific rates J Phys Chem A, 2003; 107: 794-803. J.W. Hong, J. Jeong, S.H. Kim, S. Kim, H.S. Yoon
7. Jang J, Bae J and Park E. Selective fabrication of poly (3, 4-ethylenedioxythiophene) nanocapsules and mesocellular foams using surfactant-mediated interfacial polymerization. *Adv Mater*, 2006; 18(3): 354-58.
8. Jason CHC, Jian KW, Chao MH, David Y, Huanga DY, Huangd SH, et al. Radiation induced liver disease after radiotherapy for hepatocellular carcinoma: clinical manifestation and dosimetric description. *Radiother Oncol*, 2002; 63(1): 41-45.
9. Li YP, Pei YY, Zhou ZH, Zhang XY, Gu ZH, Ding J, Zhou JJ, Gao XJ, et al. PEGylated polycyanoacrylate nanoparticles as tumor necrosis factor-[alpha] carriers. *J Control Release*, 2001; 71(3): 287-96.

10. Liu XG, Li B, Geng DY, Cui WB, Yang F, Xie ZG, et al. (Fe, Ni)/C nanocapsules for electromagnetic-wave-absorber in the whole Ku-band. *Carbon*, 2009; 47(2): 470-74.
11. Marie Curie. Novel lipid nanocapsules of anti alpha 1 sodium pump subunit SiRNA to specifically target metastatic melanomas. *European commission euraxess*, 2011; 11: 37.
12. Matkan J and Treleaven RJ. 1987. Particles containing releasable fill material and method of making same. US patent 4681806, USA.
13. Repka M. Hot Melt Extrusion. Encyclopedia of pharmaceutical technology, 2nd ed.; Swarbrick J, Boylan J (Ed.), Marcel Dekker Inc, New York, 2002; 2: 1488-1504.
14. Sangwoo P, Hong YC, Jeong YA, Yungwan K, Abiraman S, Jeffrey O, et al. Photo-Cross-Linkable Thermoresponsive Star Polymers Designed for Control of Cell- Surface Interactions. *Biomacromolecules*, 2010; 11(10): 2647-52.
15. Isolation of a Korean domestic microalga, chlamydomonas reinhardtii KNUA021, and Analysis of Its Biotechnological Potential Angew Chem, Int Ed, 2013; 52(32): 8285-8289.
16. K. Liu, Y. Liu, Y. Yao, H. Yuan, S. Wang, Z. Wang, *et al.* Supramolecular Photosensitizers with Enhanced Antibacterial Efficiency J Microbiol Biotechnol, 2013; 23: 375-381.
17. W. Yinsong, L. Lingrong, W. Jian, Q. Zhang Preparation and characterization of self-aggregated nanoparticles of cholesterol-modified O-carboxymethyl chitosan conjugates Carbohydr Polym, 2007; 69: 597-606.
18. Jurgons R., Seliger C., Hilpert A., Trahms L., Odenbach S., Alexiou C. Drug loaded magnetic nanoparticles for cancer therapy. *J. Phys. Condens. Matter*, 2006; 18: S2893. doi: 10.1088/0953-8984/18/38/S24.
19. Tocco I., Zavan B., Bassetto F., Vindigni V. Nanotechnology-based therapies for skin wound regeneration. *J. Nanomater*, 2012; 2012: 714134. doi: 10.1155/2012/714134.
20. Ashjari M., Khoee S., Mahdavian A.R. Controlling the morphology and surface property of magnetic/cisplatin-loaded nanocapsules via W/O/W double emulsion method. *Colloids Surf. A Physicochem. Eng. Asp.*, 2012; 408: 87–96. doi: 10.1016/j.colsurfa.2012.05.035. [CrossRef]
21. Campos E.V.R., Oliveira J.L., Zavala-Betancourt S.A., Ledezma A.S., Arias E., Moggio I., Romero J., Fraceto L.F. Development of stained polymeric nanocapsules loaded with model drugs: Use of a fluorescent poly(phenyleneethynylene) *Colloids Surf. B Biointerfaces*, 2016; 147: 442–449. doi: 10.1016/j.colsurfb.2016.08.031.
22. Erdmann C., Mayer C. Permeability profile of poly(alkyl cyanoacrylate) nanocapsules. *J. Colloid Interface Sci.*, 2016; 478: 394–401. doi: 10.1016/j.jcis.2016.06.034.
23. Hu S.H., Chen S.Y., Gao X. Multifunctional nanocapsules for simultaneous encapsulation of hydrophilic and hydrophobic compounds and on-demand release. *ACS Nano.*, 2012; 6: 2558–2565. doi: 10.1021/nn205023w
24. Chiang C.S., Hu S.H., Liao B.J., Chang Y.C., Chen S.Y. Enhancement of cancer therapy efficacy by trastuzumab-conjugated and pH-sensitive nanocapsules with the simultaneous encapsulation of hydrophilic and hydrophobic compounds. *Nanomedicine*, 2014; 10: 99–107. doi: 10.1016/j.nano.2013.07.009.
25. Balan V., Dodi G., Tudorachi N., Ponta O., Simon V., Butnaru M., Verestiuc L. Doxorubicin-loaded magnetic nanocapsules based on N-palmitoyl chitosan and magnetite: Synthesis and characterization. *Chem. Eng. J.*, 2015; 279: 188–197. doi: 10.1016/j.cej.2015.04.152.
26. Lu S., Xu L., Kang E.T., Mahendran R., Chiong E., Neoh K.G. Co-delivery of peptide-modified cisplatin and doxorubicin via mucoadhesive nanocapsules for potential synergistic intravesical chemotherapy of non-muscle-invasive bladder cancer. *Eur. J. Pharm. Sci.*, 2016; 84: 103–115. doi: 10.1016/j.ejps.2016.01.013.
27. Galisteo-Gonzalez F., Molina-Bolivar J.A., Navarro S.A., Boulaiz H., Aguilera-Garrido A., Ramirez A., Marchal J.A. Albumin-covered lipid nanocapsules exhibit enhanced uptake performance by breast-tumor cells. *Colloids Surf. B Biointerfaces*, 2018; 165: 103–110. doi: 10.1016/j.colsurfb.2018.02.024.
28. Molina-Bolívar J.A., Galisteo-González F. Olive-oil nanocapsules stabilized by HSA: Influence of processing variables on particle properties. *J. Nanoparticle Res.*, 2015; 17. doi: 10.1007/s11051-015-3192-1.
29. Xavier-Junior F.H., Egito E.S.T.D., Morais A.R.D.V., Alencar E.D.N., Maciuk A., Vauthier C. Experimental design approach applied to the development of chitosan coated poly(isobutylcyanoacrylate) nanocapsules encapsulating copaiba oil. *Colloids Surf. A Physicochem. Eng. Asp.*, 2018; 536: 251–258. doi: 10.1016/j.colsurfa.2017.02.055.
30. Bouchemal K., Couenne F., Briançon S., Fessi H., Tayakout M. Polyamides nanocapsules: Modeling and wall thickness estimation. *AIChE J.*, 2006; 52: 2161–2170. doi: 10.1002/aic.10828.
31. Nassar T., Rom A., Nyska A., Benita S. Novel double coated nanocapsules for intestinal delivery and enhanced oral bioavailability of tacrolimus, a P-gp substrate drug. *J. Control. Release.*, 2009; 133: 77–84. doi: 10.1016/j.jconrel.2008.08.021.
32. Rouzes C., Gref R., Leonard M., De Sousa Delgado A., Dellacherie E. Surface modification of poly (lactic acid) nanospheres using hydrophobically modified dextrans as stabilizers in an o/w emulsion/evaporation technique. *J. Biomed. Mater. Res.*, 2000; 50: 557–565. doi: 10.1002/(SICI)1097-

4636(20000615)50:4<557::AID-JBM11>3.0.CO;2-R.

33. Sahana D.K., Mittal G., Bhardwaj V., Kumar M.N. PLGA nanoparticles for oral delivery of hydrophobic drugs: Influence of organic solvent on nanoparticle formation and release behavior in vitro and in vivo using estradiol as a model drug. *J. Pharm. Sci.*, 2008; 97: 1530–1542. doi: 10.1002/jps.21158.
34. Kumar V., Prud'homme R.K. Nanoparticle stability: Processing pathways for solvent removal. *Chem. Eng. Sci.*, 2009; 64: 1358–1361. doi: 10.1016/j.ces.2008.11.017.
35. Konan Y.N., Cerny R., Favet J., Berton M., Gurny R., Allémann E. Preparation and characterization of sterile sub-200 nm meso-tetra (4-hydroxylphenyl) porphyrin-loaded nanoparticles for photodynamic therapy. *Eur. J. Pharm. Biopharm*, 2003; 55: 115–124. doi: 10.1016/S0939-6411(02)00128-5.